AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

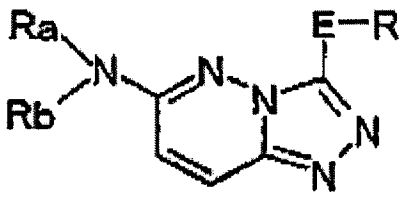
1-16. (canceled).

17. (currently amended): A method for preventing or treating a metabolic bone disease which accompanies reduction of the bone mass, ~~and/or~~ bone strength or both of bone mass and bone strength, which comprises administering to a patient an effective amount of a non-living body-derived non-peptide osteoblast differentiation promoting compound and an effective amount of a bisphosphonate, simultaneously or separately.

18. (currently amended): The method according to claim 17, wherein the metabolic bone disease which accompanies reduction of the bone mass, ~~and/or~~ bone strength or both of bone mass and bone strength is a bone metabolism turnover reducing type (type II) osteoporosis.

19-20. (canceled).

21. (previously presented): The method according to claim 17, wherein the non-living body-derived non-peptide osteoblast differentiation promoting compound is represented by the following general formula (I) or a salt thereof



(I)

(symbols in the formula have the following meanings,

Ra and Rb: the same or different and each represent H; CO-lower alkyl; SO_2-lower alkyl; an optionally substituted cycloalkyl; an optionally substituted aryl; or a lower alkyl which may have 1 to 3 substituents selected from the group consisting of an optionally substituted cycloalkyl, an optionally substituted aryl, an optionally substituted 4- to 8-membered monocyclic saturated or partially unsaturated heterocyclic ring, CO-lower alkyl, SO_2-lower alkyl, OR^1, SR^1, NR^1R^2, a halogen, NO_2, CN and $COOR^1$; provided that at least one of Ra and Rb represents a group other than H; or,

Ra and Rb taken together with an adjacent N atom form a 4- to 8-membered saturated or partially unsaturated heterocyclic ring containing 1 or 2 N atoms as heteroatoms, said heterocyclic ring may be fused with a benzene ring or a cycloalkyl ring and may have a bridge and may form a spiro ring, and said heterocyclic ring may have from 1 to 5 substituent groups,

E: a single bond, a C_{1-3} alkylene, vinylene (-C=C-), ethynylene (-C≡C-), CO, NR^3, CH_2-J, $CONR^4$ or NR^5CO,

J: O, S, NR^6, CO, SO or SO_2,

R: an optionally substituted aryl, an optionally substituted heteroaryl, an optionally substituted cycloalkyl, an optionally substituted cycloalkenyl or an optionally substituted 4- to 8-membered monocyclic saturated or partially saturated heterocyclic ring,

R^1 to R^6: the same or different and each denotes H or a lower alkyl;

with the proviso that the following compounds are excluded:

(1) a compound wherein Ra and Rb taken together with an adjacent N atom form a piperidino, E is a single bond and R is a piperidino, unsubstituted phenyl, *p*-(trifluoromethyl)phenyl, *p*-chlorophenyl or *o*-nitrophenyl,

(2) a compound wherein Ra and Rb taken together with an adjacent N atom form a 4-methyl-1-piperazinyl, E is a single bond, and R is an unsubstituted phenyl, *p*-methylphenyl, *m*-methylphenyl, *p*-methoxyphenyl, *m*-chlorophenyl, *p*-chlorophenyl or *m*-nitrophenyl,

(3) a compound wherein R is an optionally substituted imidazolyl, 5-nitro-2-furyl or 5-nitro-2-thienyl,

(4) a compound wherein Ra is H, Rb is cyclopropyl, E is a single bond and R is a *p*-(trifluoromethyl)phenyl, and

(5) a compound wherein Ra is a methyl, Rb is a 2-hydroxypropyl, E is a single bond and R is a 3-pyridyl).

22. (previously presented): The method according to claim 21, wherein the non-living body-derived non-peptide osteoblast differentiation promoting compound is a nitrogen-containing heterocyclic compound selected from the group consisting of 6-azocan-1-yl-3-(6-methoxypyridin-2-yl)-1,2,4-triazolo[4,3-b]pyridazine, 6-azepan-1-yl-3-(6-bromopyridin-2-yl)-1,2,4-triazolo[4,3-b]pyridazine, 3-(3-methoxyphenyl)-6-(piperidin-1-yl)-1,2,4-triazolo[4,3-b]pyridazine, 3-(3-bromophenyl)-6-(piperidin-1-yl)-1,2,4-triazolo[4,3-b]pyridazine, 6-azepan-1-yl-3-(6-methoxypyridin-2-yl)-1,2,4-triazolo[4,3-b]pyridazine, 6-(4-fluoropiperidin-1-yl)-3-(6-methoxypyridin-2-yl)-1,2,4-triazolo[4,3-b]pyridazine, 6-(3-azabicyclo[3.2.1]octan-3-yl)-3-(6-

methoxypyridin-2-yl)-1,2,4-triazolo[4,3-b]pyridazine, 6-(4,4-difluoropiperidin-1-yl)-3-(6-methoxypyridin-2-yl)-1,2,4-triazolo[4,3-b]pyridazine, 6-(3,3-difluoropiperidin-1-yl)-3-(6-methoxypyridin-2-yl)-1,2,4-triazolo[4,3-b]pyridazine, 6-azocan-1-yl-3-(6-bromopyridin-2-yl)-1,2,4-triazolo[4,3-b]pyridazine, and 6-(8-azabicyclo[3.2.1]octan-8-yl)-3-(6-bromopyridin-2-yl)-1,2,4-triazolo[4,3-b]pyridazine, or a salt thereof.

23. (currently amended): The method according to claim ~~21~~ 17, wherein the bisphosphonate is selected from the group consisting of alendronate, risedronate, pamidronate, incadronate, minodronate, ibandronate, and zoledronate.

24. (previously presented): The method described in claim 17, wherein the non-living body-derived non-peptide osteoblast differentiation promoting compound is 6-(4-fluoropiperidin-1-yl)-3-(6-methoxypyridin-2-yl)-1,2,4-triazolo[4,3-b]pyridazine.